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Five-Year Survival after First-Ever Ischaemic Stroke Is Worse in Total Anterior Circulation Infarcts: The SINPAC Cohort

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Key Words
Clinical stroke syndromes · Ischaemic stroke · Predictors of outcome · Stroke prognosis

Abstract
Background: Few studies have addressed predictors of long-term mortality after first-ever ischaemic stroke. ***Methods:*** We prospectively collected data on 361 consecutive patients admitted to 18 neurology departments in Italy for a first-ever ischaemic stroke in 1999, categorized according to the Oxfordshire Community Stroke Project (OCSP) classification. Age, gender, risk factors, previous vascular disease, in-hospital complications, stroke severity, functional status, therapy and living place at admission, discharge and after 6 months were recorded. Follow-up was available for 97% patients at 5 years. ***Results:*** Survival probability was 91% (95% CI = 88–94) at 1 month, 84% (80–88) at 6 months and 64% (58–69) at 5 years. Mortality was higher for the TACI (total anterior circulation infarct) group compared to the other categories ($p < 0.0001$). Hazard ratios for 5-year mortality in the final model were: 5.4 for age ≥65 years ($p < 0.0001$), 2.8 for TACI ($p < 0.0001$), 2.7 for previous vascular disease ($p < 0.01$) and 1.9 for cardio-embolic risk according to the TOAST risk stratification ($p < 0.05$). ***Conclusions:*** Our study extends the prognostic value of the OCSP classification to 5-year survival.

Introduction

Stroke is associated with high mortality in the acute phase, ranging from 13 to 27% in the first month and from 18 to 33% in the first 3 months [1]. Yet several population- [2, 3] and hospital-based [4, 5] studies have shown a 10% annual risk of death even many years after the initial stroke, i.e. twice that expected in the general population of the same age and sex. Predictors of long-term mortality for ischaemic stroke are ischaemic heart disease, atherothrombosis [6], cardio-embolic stroke [7], age and diabetes [4].

The SINPAC (Società Inter-regionale Piemonte e Valle d'Aosta per le Cerebrovasculopatie) – a group of Italian neurologists (see appendix) – has conducted a prospective study on acute cerebrovascular patients managed in neurological departments in north-western Italy during 1999. Methods and the clinical features of the population have already been described in detail [8]. We now report the results of the 6-month and 5-year follow-up of patients admitted for a first-ever ischaemic stroke classified according to the Oxfordshire Community Stroke Project (OCSP) classification [9]. We aimed to determine the variables at admission, during hospital stay, at discharge and at 6 months that independently predict survival at 5 years.

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Methods

This is a hospital-based prospective study involving 18 neurology departments (16 first-referral) of the Piedmont and the Aosta Valley Regions (north-western Italy). Patients were enrolled if older than 25 years and consecutively admitted to each department with stroke or transient ischaemic attack (TIA), either first-ever or recurrent, from May 1 to July 31, 1999. Stroke and TIA were defined according to WHO criteria [10]; subarachnoid haemorrhage was excluded.

Data were collected on a specifically designed form, including demographics, details of onset, emergency room management, risk factors, course and management during hospital stay and details of discharge. Further details on methods and design of the study are described in a previous article [8]. The choice of treatment and diagnostic work-up was left to each physician's judgement. At the time of the study, none of the participating centres had a stroke unit.

Of the 604 patients enrolled, 443 had an ischaemic stroke , 64 a haemorrhagic stroke and 97 a TIA. Here we investigate the long-term follow-up of the 361 patients with a first-ever ischaemic stroke, including 9 without CT scan accepted according to the Guy's Hospital Stroke Diagnostic Score [11]. Follow-up evaluations were scheduled at 6 months and 5 years after onset, either by clinical visit or by telephone interviews with patients, family members or caregivers. For patients not traced by the centres (47 at 6 months and 80 at 5 years), a postal follow-up was conducted through their municipality of residence: in this case, only the vital status was available. Vital status was known for 359 patients (99%) at 30 days, 357 (99%) at 6 months and 350 (97%) at 5 years; of the 11 not traced, 64% were males, the mean age was 71 ± 14 years, the mean Glasgow Coma Scale (GCS) score at admission was 14 ± 3, without any statistical difference with those who completed the follow-up (57% males, mean age 70 ± 12, mean GCS 14 ± 3). The Kaplan-Meier method was used to calculate survival curves and the log-rank test to assess differences between groups. Patients were divided according to OCSP classification into partial anterior circulation infarction (PACI), lacunar infarction (LACI), total anterior circulation infarction (TACI) and posterior circulation infarction (POCI). The other predictors were divided into the variables described below.

Pre-Admission Variables and Risk Factors

We assessed gender, age, living place, home therapy, smoking, hypertension, embolic cardiopathy according to the TOAST risk stratification [12], diabetes, hyperlipaemia, alcohol abuse, obesity, internal carotid artery occlusion/stenosis >50%, previous TIA and previous vascular disease (defined as a history of peripheral arteriopathy, deep venous thrombosis or pulmonary embolism).

In-Hospital Variables

In-hospital variables were GCS, modified Rankin Scale (MRS) and Scandinavian Stroke Study Group scale (SSS) [13] scores at admission, medical and neurological complications. Medical complications were defined as any of the following: urinary, chest or other infections, fractures, pressure sores, deep venous thrombosis, pulmonary embolism, acute pulmonary oedema, gastrointestinal bleeding or ulcer, myocardial infarction, cardiac failure, arrhythmias, peripheral arterial ischaemia, acute renal failure or painful shoulder. Neurological complications were defined as any of the following: epileptic seizure, haemorrhagic transformation, recurrent stroke, progressing stroke, depression or dementia.

Variables at Discharge

MRS score, destination and prescribed therapy were considered as variables at discharge.

Six-Month Variables

At the 6-month follow-up, MRS score, ongoing therapy and current living place were the variables assessed.

Variables were operationally defined in a previous paper [8, 14]. Missing data were handled in ways that always gave conservative estimates of each risk. Given the large number of variables that could significantly explain our outcomes, we decided to fix the α error at 0.01. Multivariate analysis (Cox proportional hazard model) was performed including the centre and the variables significant in the univariate analysis. For this purpose, the variables were dichotomized as follows: age, <65 versus ≥ 65 years; embolic risk cardiopathy, medium-to-high versus low; MRS, 1–3 versus 4–5; clinical syndrome, TACI versus all the others; destination at discharge, institution versus any other. Other variables were dichotomized as yes/no. Since GCS, SSS and MRS are associated, but only MRS was available at admission, discharge and 6 months, MRS was run in the multivariate model. Statistical analyses were performed with the SAS package version 8.2 [15].

Results

The number of strokes per centre ranged from 7 to 40. Survival probabilities were: 91% (95% CI = 88–94) at 30 days from the event, 84% (80–88) at 6 months, 81% (77–85) at 1 year, 78% (73–82) at 2, 73% (68–77) at 3, 69% (64–74) at 4 and 64% (58–69) at the 5-year follow-up (fig. 1). According to OCSP classification criteria, 125 patients (35%) had PACI, 109 (30%) LACI, 72 (20%) TACI and 55 (15%) POCI. Survival probabilities at 6 months and 5 years were significantly lower for TACI ($p < 0.0001$) compared to the other categories (table 1 and fig. 2). When considering only patients surviving the first 6 months, TACI was still predictive ($p < 0.01$; fig. 3).

Table 1 shows the survival probabilities at 6 months and 5 years for the other prognostic factors.

Pre-Admission Variables and Risk Factors

Older age, living in an institution before stroke, cardio-embolic risk and history of vascular disease were significant prognostic factors at both 6 months and 5 years.

Stroke Characteristics and In-Hospital Variables

Stroke severity at onset (evaluated either by GCS, SSS or MRS) and medical and neurological complications

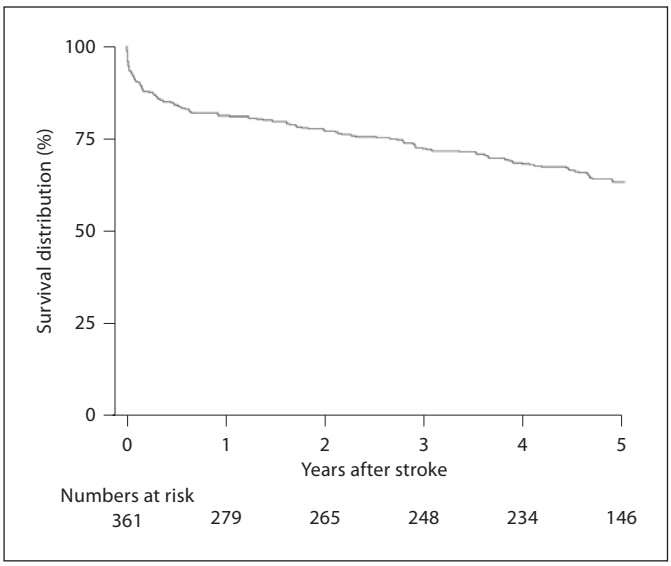

Fig. 1. Five-year overall survival for 361 patients with a first-ever ischaemic stroke.

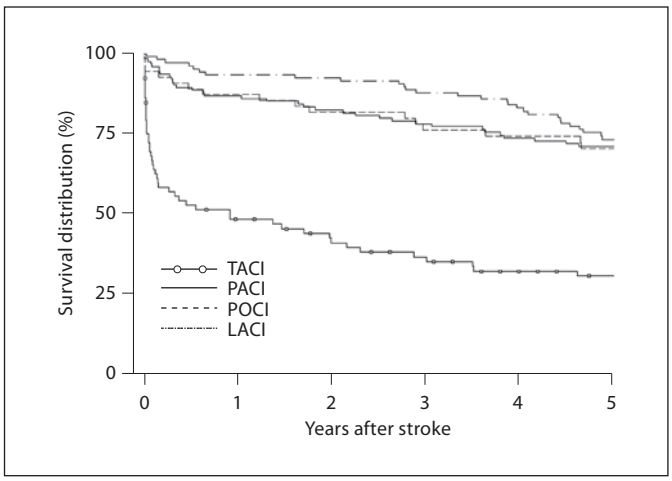

Fig. 2. Five-year survival by OCSP classification subtype. Survival times are computed from the date of stroke for PACI, LACI, TACI and POCI. TACI versus others, $p < 0.0001$; all the other comparisons are not significant.

during hospital stay were predictive of a worse survival. The first multivariate model, including centre, and those predictive pre-admission variables, risk factors, stroke characteristic and in-hospital variables significant after univariate analysis, yielded the following hazard ratios for 6-month mortality: 4.2 for TACI ($p < 0.0001$), 3.0 for MRS at admission ($p < 0.01$), 2.9 for neurological complications ($p < 0.005$), 2.1 for cardio-embolic risk ($p < 0.01$) and 2.1 for living in an institution before stroke ($p < 0.05$). Age was not retained in the model. The corresponding values for 5-year mortality were: 3.9 for age ≥65 years ($p < 0.0001$), 3.4 for TACI ($p < 0.0001$), 2.1 for neurological complications ($p < 0.01$), 2.0 for previous vascular disease ($p < 0.05$), 1.6 for cardio-embolic risk ($p < 0.01$) and 1.6 for medical complications ($p < 0.05$). The values of the likelihood ratio test of the multivariate model were 110.4 ($p < 0.0001$) at 6 months and 128.7 ($p < 0.0001$) at 5 years.

Variables at Discharge

Thirty-two patients died during their hospital stay. Among the 329 survivors, better functional status at discharge as estimated by a lower score on the MRS scale and discharge to the previous living place or to a rehabilitation unit were associated with longer survival at both follow-up times. The final multivariate models, which include the at-discharge predictors significant after univariate analysis, are shown in table 2. The values of the likelihood ratio test of the multivariate model were 38.5 ($p < 0.0001$) at 6 months and 71.8 ($p < 0.0001$) at 5 years, respectively. When considering only patients surviving the first 6 months, TACI was still an independent predictor (hazard ratio adjusted for the variables significant after univariate analysis = 2.6, $p = 0.01$).

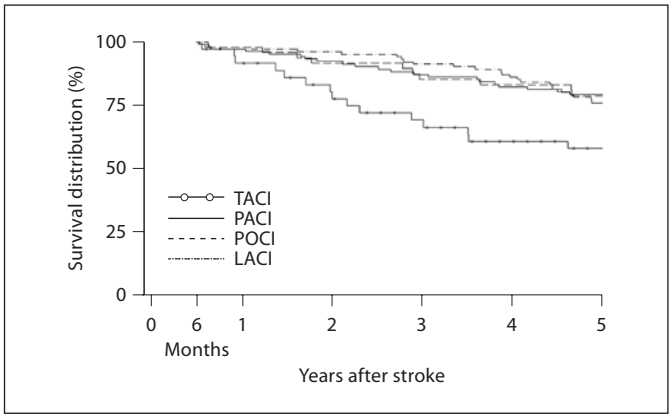

Fig. 3. Five-year survival by OCSP classification subtype for patients surviving the first 6 months. Survival times are computed from 6 months after stroke. Five-year survival percentages and 95% confidence intervals were 79.5 (71.7–87.3) for PACI, 77.2 (69.0–85.4) for LACI, 79.0 (67.4–90.6) for POCI and 58.4 (42.3–74.8) for TACI. TACI versus others, $p < 0.01$; all the other comparisons are not significant.

Table 1. Kaplan-Meier estimates of probability of survival at 6 months and 5 years after first ischaemic stroke for patients according to the study variables (univariate analysis)

	Six-month survival, %	p value	Five-year survival, %	p value
Pre-admission variables and risk factors (n = 361)				
Gender				
Female (154, 43%)	82.5 (76.4–88.6)	n.s.	60.4 (52.6–68.2)	n.s.
Male (207, 57%)	85.4 (80.5–90.3)		65.9 (59.2–72.6)	
Age				
≤64 years (101, 28%)	94.1 (89.4–98.8)		87.8 (81.3–94.3)	
65–74 years (114, 32%)	85.9 (79.4–92.4)	<0.0005	66.1 (57.1–75.1)	<0.0001
75–84 years (102, 28%)	79.3 (71.5–87.1)		49.4 (39.6–59.2)	
≥85 years (44, 12%)	67.4 (53.3–81.5)		33.8 (19.1–48.5)	
Living place				
Home (332, 92%)	85.8 (82.1–89.5)	<0.001	65.6 (60.3–70.9)	<0.001
Institution (29, 8%)	65.3 (47.9–82.7)		39.9 (21.7–58.1)	
Home therapy				
Antiplatelet drugs				
No (284, 79%)	84.4 (78.8–87.4)	n.s.	66.1 (60.4–71.8)	n.s.
Yes (77, 21%)	83.1 (74.7–91.5)		53.7 (42.1–65.3)	
Oral anticoagulants				
No (346, 96%)	84.0 (80.1–87.9)	n.s.	63.4 (58.1–68.7)	n.s.
Yes (15, 4%)	86.7 (69.5–100)		66.7 (42.8–90.6)	
Antihypertensive drugs				
No (209, 58%)	84.2 (79.3–89.1)	n.s.	61.0 (54.1–67.9)	n.s.
Yes (152, 42%)	84.1 (78.2–90.0)		66.9 (59.3–74.5)	
Oral hypoglycaemic drugs				
No (327, 91%)	84.0 (80.1–87.9)	n.s.	64.3 (59.0–69.6)	n.s.
Yes (34, 9%)	85.3 (73.3–97.3)		56.7 (39.5–74.0)	
Smoking				
No (258, 71%)	82.1 (77.4–86.8)	n.s.	60.0 (53.9–66.1)	n.s.
Yes (103, 29%)	89.2 (83.1–95.3)		72.5 (63.7–81.3)	
Hypertension				
No (147, 40%)	81.5 (75.2–87.8)	n.s.	59.3 (51.1–67.5)	n.s.
Yes (214, 60%)	85.9 (81.2–90.6)		66.4 (59.9–72.9)	
Embolic risk cardiopathy				
Low (220, 61%)	90.9 (87.2–94.6)		71.1 (65.0–77.3)	
Medium (45, 12%)	70.9 (57.6–84.2)	<0.0001	56.1 (41.2–71.0)	<0.0001
High (96, 27%)	74.6 (65.8–83.4)		48.0 (37.7–58.3)	
Diabetes				
No (297, 82%)	84.8 (80.7–88.9)	n.s.	64.8 (59.3–70.3)	n.s.
Yes (64, 18%)	81.3 (71.7–90.9)		57.9 (45.6–70.3)	
Hyperlipaemia				
No (316, 88%)	83.4 (79.3–87.5)	n.s.	62.5 (57.0–68.0)	n.s.
Yes (45, 12%)	88.9 (79.7–98.1)		70.7 (57.2–84.2)	
Alcohol abuse				
No (334, 93%)	84.0 (80.1–87.9)	n.s.	62.8 (57.5–68.1)	n.s.
Yes (27, 7%)	85.2 (71.9–98.5)		73.0 (55.8–90.3)	
Obesity				
No (303, 84%)	85.4 (81.5–89.3)	n.s.	62.6 (56.9–68.3)	n.s.
Yes (58, 16%)	77.6 (66.8–88.4)		68.3 (56.2–80.5)	
Atherosclerosis of ICA				
No (321, 89%)	83.7 (79.6–87.8)	n.s.	63.7 (58.4–69.0)	n.s.
Yes (40, 11%)	87.5 (77.3–97.7)		61.8 (45.7–77.9)	
Previous TIA				
No (315, 87%)	83.1 (79.0–87.2)	n.s.	62.5 (57.0–68.0)	n.s.
Yes (46, 13%)	91.3 (83.1–99.5)		70.7 (57.2–84.2)	
Previous vascular disease				
No (338, 94%)	85.4 (81.7–89.1)	<0.01	65.6 (60.5–70.7)	<0.0005
Yes (23, 6%)	65.2 (45.8–84.6)		34.8 (15.4–54.2)	

Table 1 (continued)

	Six-month survival, %	p value	Five-year survival, %	p value
Stroke characteristics and in-hospital variables (n = 361)				
ER GCS score				
≥14 (260, 72%)	93.8 (90.9–96.7)		74.6 (69.2–80.1)	
10–13 (56, 16%)	71.9 (60.5 – 83.3)	<0.0001	44.6 (31.6–57.6)	<0.0001
≤9 (40, 11%)	32.4 (16.7 – 48.1)		17.5 (05.7–29.3)	
MRS score at admission				
1–3 (176, 49%)	95.4 (92.3–98.5)	<0.0001	72.7 (66.0–79.4)	<0.0001
4–5 (185, 51%)	73.4 (66.9–79.9)		54.8 (47.4–62.3)	
SSS score at admission				
≥50 (127, 35%)	98.4 (96.2–100)		74.6 (66.8–82.4)	
41–49 (75, 21%)	88.0 (80.6–95.5)	<0.0001	67.2 (56.4–78.0)	<0.0001
≤40 (159, 44%)	70.9 (63.8–78.0)		53.1 (45.1–61.1)	
OCSP classification				
LACI (109, 30%)	96.3 (92.8–99.8)		73.2 (64.6–81.8)	
POCI (55, 15%)	89.1 (80.9–97.3)	<0.0001	70.4 (58.3–82.6)	<0.0001
PACI (125, 35%)	89.5 (84.0–95.0)		71.1 (62.9–79.3)	
TACI (72, 20%)	52.8 (41.2–64.4)		30.8 (20.0–41.6)	
Medical complications				
No (298, 83%)	89.9 (86.4–93.4)	<0.0001	68.9 (63.4–74.4)	<0.0001
Yes (63, 17%)	56.9 (44.6–69.3)		37.9 (25.6–50.3)	
Neurological complications				
No (330, 91%)	87.5 (84.0–91.0)	<0.0001	66.6 (61.3–71.9)	<0.0001
Yes (31, 9%)	47.5 (29.7–65.3)		30.6 (14.1–47.1)	
Variables at discharge (n = 329)				
MRS score				
1–3 (241, 73%)	95.4 (92.9–98.0)	<0.0005	74.0 (68.3–79.7)	0.001
4–5 (88, 27%)	84.1 (76.5–91.7)		57.5 (46.7–68.3)	
Destination				
Home/rehabilitation (292, 89%)	94.2 (91.5–96.9)	<0.0005	72.3 (67.0–77.6)	<0.001
Institutional care (37, 11%)	78.4 (65.1–91.7)		49.3 (32.6–66.0)	
Therapy with antiplatelet drugs/oral anticoagulants				
No (23, 7%)	92.5 (89.6–95.4)	n.s.	64.1 (44.1–84.1)	n.s.
Yes (306, 93%)	91.3 (79.7–100)		70.2 (65.7–74.7)	
Therapy with antihypertensive drugs				
No (168, 51%)	92.6 (88.5–96.7)	n.s.	68.8 (61.6–76.1)	n.s.
Yes (161, 49%)	92.3 (88.2–96.4)		70.8 (63.6–78.1)	
Six-month variables (n = 257)				
MRS score				
1–3 (221, 86%)			77.7 (72.0–83.4)	n.s.
4–5 (36, 14%)			63.7 (47.0–80.4)	
Therapy with antiplatelet drugs/oral anticoagulants				
No (21, 8%)			68.4 (47.4–89.4)	n.s.
Yes (236, 92%)			76.4 (70.7–82.1)	
Therapy with antihypertensive drugs				
No (139, 54%)			71.4 (63.6–79.2)	n.s.
Yes (118, 46%)			80.7 (73.5–88.0)	
Rehabilitation				
No (228, 89%)			73.6 (67.7–79.5)	n.s.
Yes (29, 11%)			92.9 (83.3–100)	
Living place				
As before hospital admission (231, 90%)			75.8 (70.1–81.5)	n.s.
Institution (26, 10%)			75.3 (58.0–92.5)	

Survival data in parentheses indicate 95% confidence intervals. n.s. = Non-significant; ICA = internal carotid artery; ER = emergency room.

Table 2. Six-month and 5-year survival in 361 patients with a first ischaemic stroke: final multivariate model including pre-admission variables and risk factors, in-hospital variables and variables at discharge

	Six-month hazard ratio	p value	Five-year hazard ratio	p value
Age ≥65 years	4.7	<0.05	5.4	<0.0001
TACI	3.0	<0.05	2.8	<0.001
Previous vascular disease	2.4	n.s.	2.7	<0.01
Medium-to-high embolic risk cardiopathy	4.1	<0.005	1.9	<0.005

Six-Month Variables

Twenty-five patients died between discharge and 6 months. Information on the 6-month variables was not available for 47 of the 304 survivors. There was no significant difference between patients with and without available information for age, living place, cardio-embolic risk, previous vascular disease, GCS at admission, and MRS scores at admission and discharge. Patients with missing information had more medical (21 vs. 10%, $p < 0.05$) and neurological (21 vs. 10%, $p < 0.05\%$) complications. None of the variables considered at 6 months were predictive for 5-year survival.

Discussion

In our cohort of first-ever ischaemic stroke patients hospitalized in mostly first-referral (16/18) neurological departments, the 6-month and 5-year survival rates were 84 and 64%; the major prognostic predictors of 5-year mortality were age ≥65 years, TACI stroke subtype, previous vascular disease and cardio-embolic risk.

Although many studies have estimated the short-term prognosis of first-ever ischaemic stroke, much less information is available for longer periods. Comparison with our study is hampered by differences in the case mix (first-ever vs. recurrent stroke), ascertainment (population- vs. hospital-based studies) and setting (neurological vs. medical wards). Two population-based surveys followed first-ever ischaemic patients for 5 years or more [16, 17] with a 5-year survival of 47–59%. In two hospital-based series, survival was 64% at 4 years [18] and 51% at 5 years [5]; however, the latter cohort was probably biased (age ≥65 years, Medicare subjects, ICD 436 included, first-in-the-year, not first-ever stroke). All these studies found a survival rate lower than our cohort. These differences may be real or depend on the calendar years of ascertainment (improvement of prognosis in recent years) or on a possible selection bias (inclusion of healthier and younger individuals in our neurological-ward-based study). Some studies, in fact, have shown that patients treated by neurologists have lower mortality rates [19, 20].

We used OCSP criteria to classify all our patients according to their clinical syndrome. This is a simple, easy and reliable method of categorizing acute ischaemic stroke patients and is predictive for short-term outcome [4, 21, 22]. A large European study including 2,740 first-ever ischaemic strokes [21] found a significantly higher 28-day and 3-month mortality for TACI, followed by PACI, POCI and LACI. TACI subjects had a fivefold risk of dying and a threefold risk of disability and handicap 3 months after stroke, compared to LACI. Another study [22] found a 6-month survival of 45% (TACI), 90% (LACI), 93% (POCI) and 96% (PACI). Others [23–25] reported a worse survival for TACI, still 2–3 years after stroke. We found a similar pattern still evident 5 years after stroke, when survival was only 31% for TACI and much higher for the other three groups (70–73%). LACIs have been associated with a better prognosis in many studies [26, 27]. Our survey suggests that a better long-term prognosis is not confined to LACI, since PACI and POCI also performed fairly better than TACI with a more than double survival rate, even after adjusting for the other major predictors.

We found an independent predictive value for the TOAST category of high-to-medium embolic risk cardiopathy in accordance with two large hospital-based studies from Germany [28] and the Netherlands [4]. Cardiovascular events other than cerebrovascular ones are the first cause of death in stroke survivors after the acute phase [2, 3, 29, 30]; a meta-analysis by Touzé et al. [31] found a 2% yearly risk of myocardial infarction and non-stroke vascular death after a TIA or stroke. Since a his-

tory of vascular disease was also retained in our multivariate 5-year survival models, there is reason to think that non-cerebral cardiovascular diseases may influence the long-term prognosis of stroke patients besides stroke severity characteristics.

Bae et al. [18] found that medical complications were still an independent predictor of mortality 4 years after a first or recurrent ischaemic stroke in a cohort admitted to a neurological department. In our study, mortality for patients who experienced either neurological or medical in-hospital complications was significantly higher than for those who did not in the univariate analysis, but not in the final model.

In conclusion, our study confirms the predictive value of OCSP classification at 5 years, with TACI as a strong predictive factor, associated with age, cardio-embolic risk and history of prior vascular disease. Prognostic stratification with OCSP could enhance comparability of patients in long-term trials and survival studies. Our study suffers from the selection bias inherent to a neurological-ward-based study; however, we collected consecutive patients from different centres (mostly first-referral) which makes our sample more representative of the general population, and only 3% of patients were lost to follow-up. Furthermore 42% of strokes hospitalized in the same area and year were admitted to neurology wards [8]. In addition, our employment of a hospital series allowed us to correlate long-term prognosis with many clinical predictors not available in population studies.

Acknowledgements

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Appendix: Composition of the SINPAC Group

Coordinating Committee: Sciolla R., Ferrari G., Cerrato P., Labate C., Priano L., Leone M.

Members and Collaborating Centres: Appiotti A., Priano L., Gruppallo F. (Divisione di Neurologia, Ospedale S. Andrea, Vercelli); Cerrato P., Verdun E. (Clinica Neurologica I, Ospedale Molinette, Torino); Doriguzzi C., Magliola U., Pipieri A. (Divisione di Neurologia, Ospedale E. Agnelli, Pinerolo); Bottacchi E., Corso G., D'Alessandro G. (U.O. di Neurologia, Ospedale Regionale, Aosta); De Mattei M., Rudà R. (DEA di Neurologia, Ospedale Molinette, Torino); Ferrari G., Enrico E., Maggio M. (Divisione di Neurologia, Ospedale Civile, Ivrea); Giobbe D., Palmiero R., Calvi L. (Divisione di Neurologia, Ospedale Maria Vittoria, Torino); Grasso E., Gerbino-Promis P.C., Meineri P. (Divisione di Neurologia, Ospedale Santa Croce, Cuneo); Terazzi E., Mittino D. (Clinica Neurologica, Ospedale Maggiore della Carità, Novara); Sciolla R., Gai P. (Clinica Neurologica, Ospedale S. Luigi, Orbassano); Buffa C., Cordera S., Rocci E. (Divisione di Neurologia, Ospedale S. Giacomo, Novi Ligure); Liboni W., Pavanelli E., Oddenino E. (Servizio di Neurologia, Ospedale Gradenigo, Torino); Villani A., Conte R. (Divisione di Neurologia, Ospedale S. Biagio, Domodossola); Labate C., Cristofanelli P. (Divisione di Neurologia, Ospedale Mauriziano, Torino); Provera P., Gilardengo P. (Divisione di Neurologia, Ospedale Civile, Tortona); Dutto A., Gagliano A., Cognazzo A. (Divisione di Neurologia, Ospedale Civile, Savigliano); Nobili M., Zurlo F., Vivalda L. (Divisione di Neurologia, Ospedale Martini, Torino); Ravetti C., Lovera N., Chianale G. (Divisione di Neurologia, Ospedale G. Bosco, Torino).

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